

CLINICAL PATHOLOGY IN GENERAL PRACTICE**INFECTED URINE**

BY

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One of the commonest reasons for suspecting a urinary infection is because the urine appears turbid, but this may, of course, be due to other factors than bacterial infection.

It is generally possible to decide fairly quickly whether or not turbidity is due to infection or to other causes. A turbidity which disappears on warming is due to urates only, but if the turbidity remains after the test-tube has been warmed then another sample should be taken and a few drops of acetic acid added, because a cloudiness which clears up with acetic acid only is due simply to phosphates. If the turbidity persists both after warming and after acidifying with acetic acid then it is probably due to pus, to blood, or to bacteria. Urine that is "bell clear" in appearance is very seldom infected.

Microscopical Evidence of Infection

The presence of infection is confirmed by the detection of pus or bacteria in the urine. An infected urine generally contains pus cells, and microscopical examination is the only way of identifying these. Chemical tests for pus are so insensitive and open to so many fallacies that they are hardly worth performing.

The simplest and quickest way of carrying out the microscope test is to take a drop of the urine and run it into the chamber of a Fuchs-Rosenthal slide, such as is used for the examination of cerebrospinal fluid. This differs from the ordinary blood-count slide in that it is ruled to enclose 16 mm.² and has a depth of 0.2 mm., whereas the haemocytometer slide is only 0.1 mm. in depth.

If a drop of urine is pipetted into such a C.S.F.-counting chamber and allowed to settle it can be examined in a few moments, and microscopical examination will show at once whether or not the urine contains pus or blood. One great advantage of this method is that no centrifuging is necessary. Another is that one can decide at once whether the turbidity of the urine is due to pus, blood, bacteria, or crystals, and, if pus is present, roughly how much there is.

The more usual method of carrying out a microscopical examination is first to centrifuge the urine, then to place a drop of the deposit on an ordinary microscope slide, cover this with a cover-glass, and examine with the sixth objective. This is certainly the best method, but if no centrifuge is available the urine may be allowed to stand in a conical vessel for a few hours until a deposit has formed. After decantation of the supernatant urine a drop of the deposit is collected in a pipette and examined on a slide beneath a cover-glass.

Before passing on to bacteriological tests it is worth recalling that sometimes tests for pyuria may give an indication of the location of the infection in the urinary tract. The two-glass test is often sufficient for deciding whether pus comes from the urethra or the bladder. To perform this test the patient is asked to pass urine into two glasses. Pus present in the first glass is assumed to be derived from the urethra, and that in the second from the bladder or kidneys.

In suspected pyelitis or pyelonephritis and in some cases of renal tuberculosis it may be necessary to examine specimens of urine collected separately from the bladder and each kidney. A unilateral tuberculous lesion of the kidney gives rise to pyuria from the affected kidney, whilst the

urine from the opposite kidney and the bladder is clear. Uncomplicated cystitis shows the presence of pus in the bladder urine, but the urine from each kidney is free from pus and sterile. When large quantities of pus are found in urine this is almost always due to cystitis. Pyelitis, pyelonephritis, prostatitis, and urethritis usually give rise only to a relatively slight degree of pyuria.

Collection of Specimens for Bacteriological Tests

Specimens of urine for bacteriological examination need to be collected with special care and to be examined as soon as possible. Catheterization is not always necessary. For male patients a mid-stream specimen collected after cleansing the urethral orifice is generally quite satisfactory for bacteriological tests. Catheterization is more often required with female patients; in fact, if urine from women is found to contain a few pus cells and bacteria a catheter specimen is generally necessary in order to decide whether or not infection is present. Naturally catheterization should be avoided if possible, and it is worth pointing out that with reasonable care a clean specimen can often be obtained from a woman patient. A preliminary examination of this may be enough to decide whether or not catheterization will ultimately be necessary. The collection of a "clean" specimen of urine from infants or young children is a task which may tax the ingenuity and resources of all concerned.

Microscopical Examination of Stained Films

The next step is the examination of stained films from the centrifuged deposit, and for the preparation of these a drop of the deposit is spread evenly over a microscope slide and allowed to dry. The film is then fixed with heat by passing it three times through a flame. All urinary deposits should be stained with Gram's method as a routine. The great advantage of this stain is that it distinguishes between staphylococci, which are Gram-positive and appear purple in the stained film, and gonococci, which are Gram-negative and stain red. It is useful also in distinguishing the common Gram-positive diphtheroids and Döderlein's bacilli from Gram-negative bacilli such as *Bact. coli*, etc.

Whether or not any other stains should be used depends on the nature of the case. If there is no reason to suspect tuberculosis or other unusual infection, it is not necessary as a rule to stain more films. On the other hand, if the Gram stain shows the presence of pus cells but no bacteria, or if tuberculosis is suspected, the films should be stained by one of the methods used for acid-fast bacteria. Tubercle bacilli are rarely found in large numbers in the urine, and it may take several minutes' search to find them in a stained film, but bacteria like staphylococci, *Bact. coli*, and other coliform organisms are present in such large numbers that they can be recognized by one glance at the stained film.

Bact. Coli Infections

Infection with *Bact. coli* is a common finding. It may give rise to infections of the kidney, bladder, prostate, or epididymis, each of which has its own distinctive symptomatology. When the urine is found to be infected with *Bact. coli* the next step is to discover which part of the urinary tract is affected. This may generally be decided from the clinical history and the results of physical examination, but in exceptional cases it can be determined only after the collection of urine from the bladder and each kidney separately.

Meanwhile the problem remains, why has the infection occurred? *Bact. coli* is a relatively harmless microbial species and rarely causes trouble in organs which are functioning normally, so it becomes the object of clinical examination not only to decide where the infection is located but also why this region is affected. Many *Bact. coli* infections of the urinary tract are unlikely to be permanently cured until some underlying structural or functional defect has first been removed. Special predisposing causes are peculiar to different periods of life, such as infancy, pregnancy, or the years when prostatic obstruction is apt to set in.

Urine infected with *Bact. coli* is hazy when passed and has an opalescent appearance. If the urine glass or bottle is held up to the light and rotated to circulate the urine, the haziness appears like a drifting mist, a very characteristic feature. This is caused by the innumerable bacteria suspended in the urine. The haziness of the urine varies in intensity in different samples, being most evident in the early-morning urine. Later in the day the urine may be almost clear. The hazy opalescent appearance is only found in samples of urine almost free from pus. If much pus or blood is also present it will cause a turbidity which conceals the characteristic appearance of a simple bacilluria. In some cases of *Bact. coli* infection the urine has a peculiar fishy odour, but this is not invariably characteristic. The faculty of smell is rarely used as an aid to diagnosis in any branch of medicine nowadays, and without being fastidious most of us would agree with the views of the seventeenth-century physician who wrote: "It is too base and sometimes dangerous for the physician to put his nose to the urine to discern the stench thereof."

Proteus and Pyocyanus Infections

Urine infected with proteus has the same general appearance as in *Bact. coli* infections but may also contain a small quantity of viscid ropy mucus in which the pus cells are suspended. The reaction is usually alkaline, and triple phosphate crystals and amorphous phosphates are commonly found in the deposit.

Infections with proteus may occur either in the bladder or in the kidney and are generally of a more severe character than *Bact. coli* infections, and more difficult to cure. *Ps. pyocyanus* is found in the urine under similar circumstances to *B. proteus*. If pus is present in large quantity this may develop a bluish green colour on standing.

Staphylococcal and Streptococcal Infections

The presence of staphylococci in urine may be the result of chance contamination in collection, and it is common to find these and other bacteria in any stale specimen which has begun to undergo ammoniacal fermentation. In these circumstances, of course, the presence of staphylococci is of no pathological significance; but if they are recovered from urine which has been carefully collected and examined without delay the finding of these organisms is an important observation. Staphylococcal infections may occur in the kidney, bladder, prostate, urethra, and epididymis. They may be associated with calculous disease and provide evidence of both the existence and the nature of a stone. The examination of stained films from the centrifuged deposit of the urine is a test which should never be omitted in calculous disease. In stones associated with staphylococcal infections the films may show enormous numbers of Gram-positive cocci, though the bacteriological culture plates may yield only a few colonies. When the urine is infected with staphylococci or proteus, and is strongly alkaline in reaction, further tests should be carried out to see whether or not the infecting bacteria ferment urea. Most strains of staphylococci and proteus ferment urea and thus render the urine alkaline, leading to the precipitation of phosphates and calcium carbonate.

Streptococcal urinary infections are rare, but it is fairly common to find streptococci in the urine in mixed infections, especially in severe urinary sepsis associated with carcinoma of the bladder or vesico-colic fistula. Pure streptococcal

infections of the urine may be found in cases of pyaemic abscess of the kidney and chronic urethritis and prostatitis.

Gonococcal Infections

Three laboratory tests may be used in the diagnosis of gonorrhoea—namely, microscopical examination of films, bacteriological examination of cultures for gonococci, and the gonococcal complement-fixation test. The film method is usually sufficient for the recognition of acute gonorrhoea, but in chronic infections it is best to make use of both films and cultures. This is especially important when the finding of Gram-negative diplococci in films is an unexpected observation, and also in tests for cure in chronic gonorrhoea. In all medico-legal cases all three methods of examination should be employed. These tests will be discussed in more detail in a later article in this series.

Urinary Tuberculosis

Three methods are available for the detection of tubercle bacilli in urine: stained films, cultures, and animal inoculation.

The film method is the easiest and requires least apparatus. It has the advantage that it takes only a few minutes to carry out, and so a report can be given without delay. The tubercle bacillus is the only pathogenic acid-fast bacillus likely to be present in the urine, and with proper precautions it is unlikely that a trained observer will report a false positive by mistaking one of the non-pathogenic acid-fast bacilli for the tubercle bacillus. The stained film is therefore the regular routine method of examination. If acid-fast bacilli having the typical morphological characters and staining reactions of tubercle bacilli are found in stained films in association with red blood cells and pus, then, as a general rule, no further tests are necessary, and the diagnosis of tuberculosis may be considered to be established. If acid-fast bacilli are found which are not quite typical in microscopical appearances, then it is best to reserve a final opinion until the results of the cultures are available, or until virulence tests have been undertaken. On the other hand, when acid-fast bacilli are found in a urinary deposit unaccompanied by blood cells or pus then it is always necessary to proceed to confirmatory tests before accepting these acid-fast bacteria as genuine tubercle bacilli.

Culture tests for tubercle bacilli are not difficult to carry out and are a routine procedure in hospital laboratories. They are useful for the further study of acid-fast bacilli of uncertain character found in films. They should also be undertaken in cases in which there is a possibility of a tuberculous infection although acid-fast bacilli have not been found in the stained films. In a small percentage of cases of urinary tuberculosis tubercle bacilli may be obtained from cultures when they could not be found by examination of films. This is because the pathologist can plant out on the culture media a much larger volume of urine than could be searched in a film; therefore, when tubercle bacilli are relatively scarce it is only to be expected that some cultures may be positive when the films have been negative.

Guinea-pig inoculation is the final court of appeal in tuberculosis, but it should not be resorted to unless other methods of diagnosis have failed. It is an expensive test, it takes at least three to six weeks to complete, and it involves an experiment on a living animal which, naturally, should only be undertaken with reluctance. Experience has shown that the guinea-pig inoculation test very rarely reveals the presence of tubercle bacilli which could not have been discovered by films or by cultures. In fact the culture method is probably a more delicate test than guinea-pig inoculation, especially when large quantities of the centrifuged deposit of urine are spread over several culture tubes. By this distribution of the centrifuged deposit it is possible to submit for examination a larger volume of urine than can be injected into one guinea-pig. However, there are certainly some occasions when animal-inoculation tests are indispensable—for example, in identifying suspicious acid-

fast bacilli recovered by culture, and in the examination of material which is limited in quantity and obtained with special difficulty, such as urine collected by catheterization of the ureters.

Sensitivity Tests

The range of antibiotics is steadily extending, consequently there is an increasing demand on the services of the laboratory for carrying out sensitivity tests in cases of urinary infection. It is well established that most staphylococci and streptococci recovered from urinary infections are sensitive to penicillin whereas *Bact. coli* and other coliform organisms are generally insensitive to penicillin, though often sensitive to chloramphenicol, aureomycin, or oxytetracycline. If the urine is infected with *B. proteus* or *Ps. pyocyanea* response to oxytetracycline or streptomycin may be expected in some cases. The laboratory control of chemotherapy will be discussed more fully later in this series.

Next article on Clinical Pathology.—"Tests of Renal Function," by Dr. R. I. S. Bayliss.

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THE LIBRARY OF THE ROYAL SOCIETY OF MEDICINE

An extension to the library of the Royal Society of Medicine is being opened this week, on Friday, December 4, by the Marquess of Salisbury. The new library, which is to be called the Wellcome Research Library, has been provided through the generosity of the Wellcome Trustees. To celebrate this occasion we have pleasure in printing below an authoritative account by a special correspondent of the origin and growth of the library of the Royal Society of Medicine.

The Royal Society of Medicine was founded in 1907 following the amalgamation of a number of specialist medical societies and the Royal Medical and Chirurgical Society of London. Some of the special societies had built up collections of books, but the chief foundation of the library of the Royal Society of Medicine was the library of the Royal Medical and Chirurgical Society of London. It is impossible to neglect the history of the library of the R.M.C.S. in any account of the library of the R.S.M., and even to-day some of the library regulations of the parent society remain unchanged.

Foundation of the R.M.C.S. Library

According to the first minute of the meeting which led to the foundation, in 1805, of the Medical and Chirurgical Society of London it was "Resolved unanimously that a society comprehending the several branches of the medical profession be established in London, for the purpose of conversations on professional subjects, for the reception of communications and for the formation of a library." When the first secretary, John Yelloly, reported on "the dignified and important objects for which this society has been established" he placed high among them "the collection of an extensive and select professional library." A library committee was set up in 1806, when £100 was provided to buy books. Presentations were received, and by 1808 the library had about 500 volumes.

The First Honorary Librarian

In 1810 the Society moved from its first house at 2, Verulam Buildings, to 3, Lincoln's Inn Fields, which was

shared with the Geological Society. The growth of the library was not forgotten at this time, for the Medical and Chirurgical Society obtained the right to erect bookcases in the meeting-room. Some members had already shown an interest in "arranging the library," and in 1812 Bateman was appointed honorary librarian; he thought highly enough of his office to mention it on the title-page of his *Delineations of Cutaneous Diseases* (London, 1817). James Atkinson in his *Medical Bibliography* has left this description of the first honorary librarian: "He was then [i.e., a year before Bateman's death] a spare, oblique, marasmoid figure, labouring much under disease, and a cornucopia of whims and self-possession or conceits; but of a very irritable kind. He then gave me the idea that he never could have been the quiet discreet registrar of disease, which bears so much semblance in his works, and I confess that from the state of exuvium in which I saw him, I should have set him down for anything but a clever man—I mean, in science, as an *homo saturatim imbutus*. We must recollect, however, that when any man is unwell, it is not the time to take his portrait." Soon after his appointment, Bateman, in company with Yelloly, made a book-buying journey to Paris, and the library benefited greatly from this.

The first printed catalogue was issued in 1816. Two years later a supplement appeared and a library copy formed from these and kept up to date by the insertion of new entries remained in use for many years. This same period saw the establishment of practices which are still followed to-day. In 1817 the number of volumes which a member might borrow was raised to eight, though new books and journals less than a month old could not be borrowed. In 1818, with the appointment of Samuel Cooper to assist Bateman, the custom was established of entrusting the supervision of the library to two honorary librarians. A third point of present-day practice also dates from this time. It was ordered in 1816 that a written request from the member concerned must be presented by anyone claiming to be borrowing books on his behalf; this was after "a person unknown had taken out books in Dr. Goode's name."

In 1819 the Society moved to 30, Lincoln's Inn Fields, and in 1820 to number 57, where it remained for the next 14 years. There is no known record of the effect on the library of these repeated removals, but the occurrence of unusually high binding costs at this time suggests that the books suffered physical damage.

In 1822 the Council ordered that "all new English publications be sent in as soon as published, subject to their being returned to the booksellers, if presented by the authors to the Society." This practice was modified in 1826, when the Council ordered that books laid before it for approval should have been seen by one of the librarians and "sent forward with his sanction."

For some years it seemed to have been one of the duties of the resident clerk "to deliver out the books," but in 1832 an "assistant to the librarians" was first employed, apparently solely for library duties under the supervision of the librarians.

In 1835, when the Society moved to 53, Berners Street, a reviewer in the *Lancet* of April 23 made some harsh criticism of London medical libraries in his notice of Forbes's *Medical Bibliography*. He said of the R.M.C.S. library: "It is only lately that any French journals have been added: no German or Italian, or any other continental medical journal beside the French is now received. Only a minority of modern works, and those slowly, are procured. . . . The utmost ignorance of foreign medical literature evidently prevails among the managers." A new catalogue was started in 1837, and a copy was distributed to every Fellow in 1844. By 1847 storage space was giving concern, but the deficiencies in the collections were an even greater anxiety. A committee of 21 Fellows was created to inquire into these deficiencies and to prepare lists of books for purchase. As a result, 432 books (57 English, 153 French, 175 German, 5 Italian, and 42 Latin) were bought in 1848 at a cost of £253 10s. 9d.